Træf for Organisk Kemi-Studerende

TOKS XVI

Aarhus University 2017

November 3rd & 4th 2017

Department of Chemistry
Aarhus University

BioNEC

IDA

AARHUS UNIVERSITY

CADIAC
CARBON DIOXIDE ACTIVATION CENTER

KEMISK FORENING
DANISH CHEMICAL SOCIETY

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Programme TOKS XVI

Aarhus University 2017

Friday 3rd of November

11_{00} Registration and lunch

12_{00} Opening of TOKS XVI: Prof. Kurt V. Gothelf

Session 1: Prof. Troels Skrydstrup

12_{15} External speaker 1: Prof. Naoto Chatani

13_{15} Break

13_{30} Student presentations

- Raoul Walther
- Martin Kilde
- Jakob Blom

14_{30} Poster session 1 (sponsored by IDA)
(*Even numbers present*)

Session 2: Prof. Kim Daasbjerg

15_{15} External speaker 2: Prof. Matthias Beller

16_{15} Break

16_{30} Student presentations

- Frederik Jørgensen
- Matteo Miola
- Cedrick Veryser

17_{30} Poster session 2
(*Odd numbers present)*

18_{30} Dinner at Mathematical canteen (see p. 42 for route directions)

Saturday 4th of November

9_{30} Coffee

Session 3: Prof. Thomas B. Poulsen

10_{00} External speaker 3: Prof. Thomas Magauer

11_{00} Break

11_{15} Student presentations

- Emilie Underlin
- Mikkel Skovsgaard
- Nikolaj Villadsen

12_{15} Lunch at Mathematical canteen

Session 4: Prof. Troels Skrydstrup

13_{15} External speaker 4: Dr. Fabrice Gallou

14_{15} Closing remarks

14_{30} End of TOKS XVI

Professor Naoto Chatani

From the Faculty of Engineering, Osaka University, Japan, the Japanese guru of C-H activation Prof. Naoto Chatani has come to TOKS to give a lecture. Prof. Chatani has spent most of his academic career at Osaka University. After graduating with a PhD in 1984 he received a position of Assistant Professor at Osaka University from 84-88, before moving to University of Illinois (USA) as a post-doctoral fellow under the supervision as Prof. Scott E. Denmark. He later returned to Osaka University where he received the Full Professor title in 2003.

Prof. Chatani is famous worldwide for his carefully designed activation of some of the most unreactive bonds. This includes both aromatic, vinylic and aliphatic C-H bonds, as well as C-C, C-F, and C-O. Within this exciting field Prof. Chatani has published in high end journals such as Nature and Science receiving more than 7500 overall citations.

Outside academia Prof. Chatani is fond of historical literature and sake. As he said in an interview published in a special edition of Angewandte Chemie: "*There are as many different types of Sake as there are European wines. (…) When I'm frustrated, I have some Sake to make me relax a bit and then get some rest."* (Angew. Chem. Int. Ed. 2017*, 56,* 8042).

Topics of interest:

Catalytic Activation of Unreactive Bonds such as C-H, C-C, and C-F

Efficient capture of reactive intermediates

Catalytic Cycloadditions

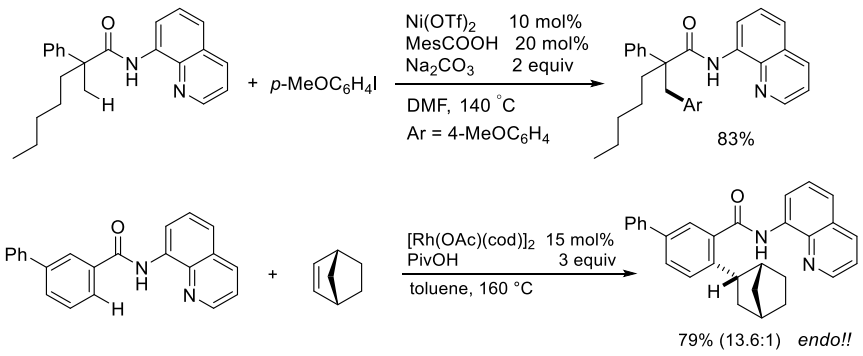
FUNCTIONALIZATION OF C-H BONDS USING BIDENTATE DIRECTING GROUP

Naoto Chatani

Department of Applied Chemistry, Faculty of Engineering, Osaka University,

Suita, Osaka 565-0871, Japan. chatani@chem.eng.osaka-u.ac.jp

The transition-metal-catalyzed C-H functionalization reactions have attracted widespread attention in the field of organic synthesis due to its high efficiency and atom economy. The regioselective C-H functionalization can be achieved by chelation-directed metalation using a directing group. The most important role of the directing group in chelation-assisted C-H functionalization reactions is to permit the catalyst to come into close proximity to the C-H bond, resulting in the formation of a stable 5- or 6-membered metalacycle. Although a wide variety of directing groups has been developed to date, the design of new types of directing groups continues to be important in terms of developing new types of C-H functionalization reations that cannot be achieved when commonly used directing groups are used. In fact, the use of bidentate-chelation systems in C-H functionalizations has attracted a great deal of interest.[1] I will present the Ni- and Rh-catalyzed C-H functionalization taking advantage of an 8-aminoquinoline chelation-assisted system.



[1] For our recent reviews on C-H functionalization using a bidentate directing group, see: G. Rouquet, N. Chatani, *Angew. Chem. Int. Ed.* **2013**, *52*, 11726. L. C. Misal Castro, N. Chatani, *Chem. Lett.* **2015**, *44*, 410. N. Chatani, *Top. Organomet. Chem.* **2016**, *56*, 19. Y. Kommagalla, N. Chatani, *Coord. Chem. Rev*. in press (https://doi.org/10.1016/j.ccr.2017.06.018).

Professor Matthias Beller

Professor Matthias Beller is head of the Department of Applied Sustainable Catalytic Processes at the Leibniz-Institut Für Katalyse (LIKAT) located in Rostock, Germany, one of the largest publicly funded research institutes in Europe. Prof. Beller started his career in the group of Prof. Dr. D. L. Tietze at University of Göttingen, Germany. After graduating in 1989 he did a post-doctoral study at Massachusetts Institute of Technology (USA) under the supervision of Nobel Prize winner Prof. K. Barry Sharpless. His Full Professor title was obtained in 1998 along with the position as director of Leibniz-Institut für Organische Katalyse at the Universität Rostock (IoFK) which was later renamed LIKAT.

As head of department Prof. Beller is involved in several ongoing projects concerning topics such as organic chemistry, electrochemistry, photochemistry, and theoretical calculations. Consequently, picking one specific topic for his talk has not been an easy task, as by this day Prof. Beller has published 843 articles. Some of the highlights in his career regarding organic chemistry has been the development of cyclometalated palladium catalysts for efficient Suzuki reactions, the first palladium(0) carbene complex, and an efficient formylation protocol of aryl and heteroaryl halides.

Topics of interest:

Applied Sustainable Catalytic Processes

Innovative Methods and Technologies in Catalysis

Special (Metal)Organic Syntheses and Catalysis

Unifying Concepts for Homogeneous and Heterogeneous Catalysis: Teaching Base Metals to behave like Noble Metals

Matthias Beller, Leibniz-Institut für Katalyse an der Universität Rostock, Albert-Einstein-Str. 29a, 18059 Rostock, Germany, matthias.beller@catalysis.de

The cost-effective and waste-free synthesis of materials, life science goods and all kinds of organic products require efficient chemical transformations. In this regard, development of more active and selective catalysts constitutes a key factor for achieving improved processes and providing the basis for a sustainable chemical industry. Despite continuous advancements in all areas of catalysis, still organic syntheses as well as the industrial production of most chemicals can be improved significantly in terms of sustainability and efficiency.

In the talk, it will be shown how new and improved homogeneous and heterogeneous catalysts can be developed by learning from each other. Specifically, the phenomenon of cooperative catalysis will be addressed in the context of non-noble metal-based catalysts. In detail, it will be demonstrated that recently developed molecular-defined as well as nano-structured cobalt and iron catalysts enable catalytic (de)hydrogenation processes with high yields and unprecedented selectivity. Examples which demonstrate the potential of such catalytic processes with bio-relevant metal complexes compared to more traditional catalytic reactions will also include reactions for energy technologies.

Selected references:

[1] X. Cui, A.-E. Surkus, K. Junge, C. Topf, J. Radnik, C. Kreyenschulte, M. Beller, *Nature Communications* **2016**, *7*, 11326.

[2] a) F. Westerhaus, R. Jagadeesh, G. Wienhöfer, M.-M. Pohl, J. Radnik, A.-E. Surkus, K. Junge, H. Junge, M. Beller, *Nature Chem.* **2013**, *5*, 607-612; b). K. Natte, H. Neumann, R. V. Jagadeesh, M. Beller, *Nature Communications* **2017**, *8*, in press.

[3] M. Nielsen, E. Alberico, W. Baumann, H.-J. Drexler, H. Junge, S. Gladiali, M. Beller, *Nature* **2013**, *494*, 85-89.

[4] C. Bornschein, S. Werkmeister, B. Wendt, H. Jiao, E. Alberico, W. Baumann, K. Junge, M. Beller *Nature Communications* **2014**, *5*, 4111.

[5] a) R. V. Jagadeesh, H. Junge, M. Beller, *Nature Communications*, **2014**, *5*, 4123.

Professor Thomas Magauer

Prof. Magauer from the University of Innsbruck, Austria, has advanced quickly during his relatively short career. Prof. Magauer has been interested in the synthesis of complex natural products. He did his PhD in Vienna on polyketide synthesis. After graduating in 2009, Prof. Magauer did a post-doctoral study at Harvard University (USA), where he studied under the supervision of Prof. Andrew G. Myers, focusing on carbohydrate chemistry. In 2012 Prof. Magauer returned to Europe where he started his independent research group at LMU Munich (Germany) – before being appointed Full Professor at the University of Innsbruck (Austria) in August 2017, less than a decade after his PhD studies!

Since the beginning of his career Prof. Magauer's inspiration has come from the large library of natural products, which remain unexplored due to their complex architectures. In the pursuit of a synthetic pathway towards bioactive molecules Magauer, seeks to invent new methodologies, applicable for retrosynthetic bond disconnections in total synthesis. In addition, the group is not afraid to start a mechanistic study whenever a better understanding of reactivity and selectivity is required.

Topics of interest:

Arenes and Halogenated molecules

Polyfunctionalized Natural Products

Trihaloethenes as Versatile Building Blocks for Organic Synthesis

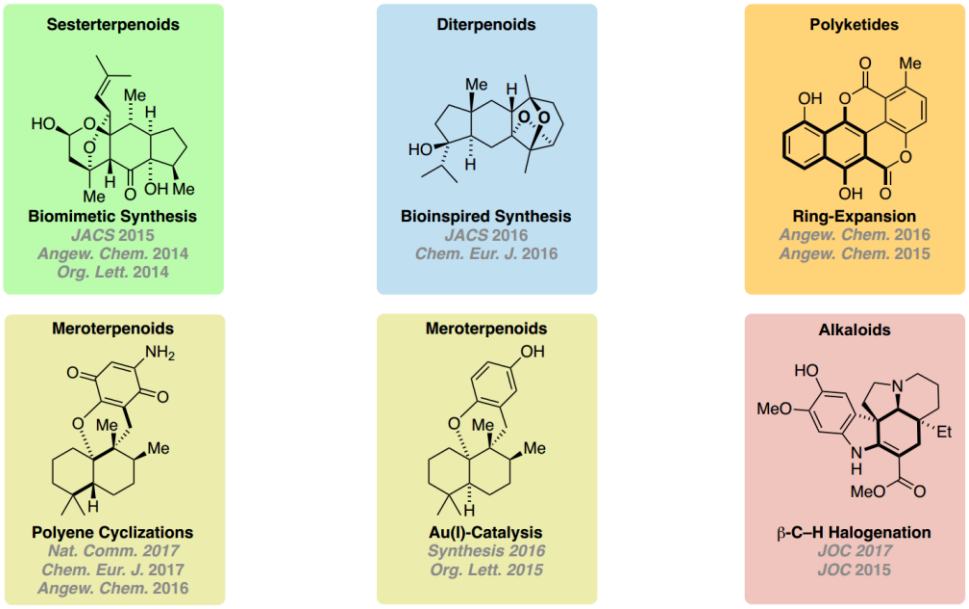
Construction and Deconstruction of Three-Dimensional Molecules

Thomas Magauer, Full Professor of Synthesis and Synthetic Methods

Centre of Chemistry and Biomedicine

Department of Organic Chemistry

Leopold-Franzens-University Innsbruck



Natural products constitute a vast and largely unexplored library of complex molecular architectures, and are a fundamental source for novel bioactive agents. However, the complex architecture of these molecules often prevents their application in medicinal chemistry. For us, this is an inspiration to think about bioinspired retrosynthetic bond disconnections which enable rapid access to the target compounds. We want to discover, design, and develop powerful transformations and apply them to the synthesis of biologically relevant complex natural products and simplified analogs thereof. The goal of these projects is to shed light on proposed biosynthetic processes, to identify new molecular targets and ultimately provide new lead compounds for the treatment of human diseases.

Dr. Fabrice Gallou

Representing Novartis Pharma's headquarters in Basel, Switzerland, Scientific Officer for the Chemical Development Dr. Fabrice Gallou will present the alternative career path outside academia. Dr. Gallou obtained his PhD at Ohio State University in 2001 in the field of natural products total synthesis. Afterwards he joined the Boehringer Ingelheim, USA, before starting his career at Novartis, Switzerland, in 2006. He has a scientific track of record with more than 110 patents and peer reviewed publications.

Novartis globally manufacture a large selection of different drugs for treatment of nearly as many diseases. However, new active pharmaceutical ingredients (APIs) is still called for. Dr. Gallou's research involves the development and implementation of efficient syntheses and processes in order to expand the portfolio of APIs. Dr. Gallou is involved in several projects, and still publishes articles on topics such as catalysis, upscaling and solvent effects.

Topics of interest:

Catalysis in the Medicinal Industry

Upscaling Chemical Reactions

Switching from Organic to Aqueous Solvents

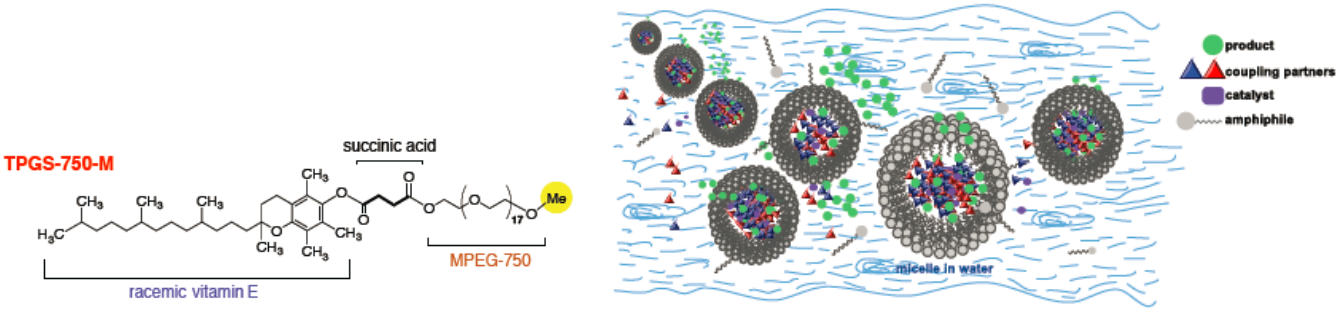
Alternative solvents: from a compliance-driven activity to a trigger for innovation

Fabrice Gallou

Chemical & Analytical Development, Novartis Pharma AG, 4056 Basel, Switzerland.

E-mail: fabrice.gallou@novartis.com

During our evaluation of the potential of surfactant technology in collaboration with Professor Lipshutz,[1,2] we have identified a variety of straightforward and highly advantageous transformations and applied them successfully on-scale.[3] Implementation of the technology typically results into significant benefits across our entire portfolio, not just from an environmental standpoint but also from an economic and productivity perspective. To name a few: Reduction of organic solvent consumption, water use and cycle time, milder reaction conditions, improved yields and selectivities, which all contribute to improved process performance and lower manufacturing costs.[4]



Modern no-ionic surfactants for micellar catalysis in water.

These surfactant mediated reactions can be up-scaled in the already existing multi-purpose facilities of pharmaceutical or chemical organizations, using a catalytic amount of a combination of a non-ionic designer surfactant (e.g. TPGS-750-M) in water, and a well-chosen organic co-solvent instead of traditional and undesirable organic solvents.[5]

Recent applications and future development will be presented.

[1] See for example: *Science* **2015**, *349*, 1087; *Ang. Chem. Int. Ed.* ***2016****, 55, 8979; Ang. Chem. Int. Ed.* ***2016****, 55, 4914.*
[2] *J. Am. Chem. Soc*. **2013**, *135*, 17707; *Org. Lett*. **2015**, *17*, 4734; *Org. Lett*. **2015**, *17*, 3968; *Org. Proc. Res. Dev*. **2016**, *20*, 1104.
[3] *Green Chem.* ***2016****, 18, 14.*

[4] *ACS Sustain Chem. Eng*. **2016**, asap.

[5] *Org. Proc. Res. Dev*. **2016**, *20*, 1388.

Student presentation 1

Fluoroquinolone glucuronide prodrugs: design, synthesis and *in vitro* validation.

Raoul Walther[1], Rikke Christiansen[2], Rikke Louise Meyer[2], Alexander Zelikin[1,2]
[1]Department of Chemistry, Aarhus University, Denmark; [2]iNano Interdisciplinary Nanoscience Centre, Aarhus University, Denmark

Postoperative bacterial infections caused by medical implants or by medical devices are attributed to 64% of all acquired infections worldwide. Strategies for preventing bacterial infections through design and modulation of biomaterials are an emerging field, and herein biocatalytic polyelectrolyte coatings are envisioned to give superior tunability, and control than conventional antibacterial coatings. Enzyme-prodrug-therapy (EPT) incorporated into surface coatings enable various tunable properties, including on-demand localized drug release, dosage, and duration (Figure 1, left). Moreover, alternative antibacterial strategies are quintessential for keeping emergence of antibiotic resistance at bay due to antibiotic discovery being an immensely challenging field by its own rights. Herein a prodrug strategy presents an ideal platform to overcome emergence of bacterial resistance.

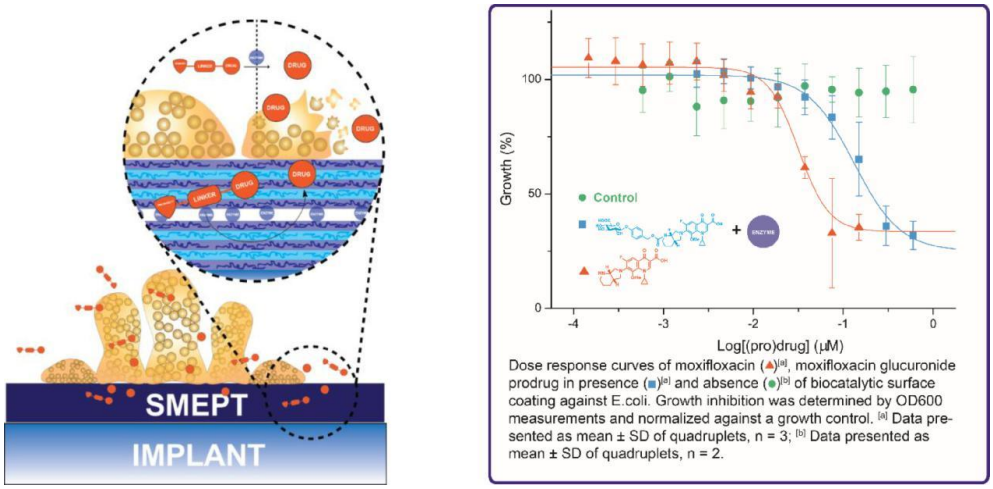


Figure 1: Schematic illustration of biocatalytic surface coating for the treatment of implant associated biofilm infection (left); Dose response curve of fluoroquinolone glucuronide prodrugs against E. Coli (right).

The development of substrate-mediated-enzyme-prodrug-therapy (SMEPT) as an alternative strategy for antibacterial coatings in conjunction with fluoroquinolone glucuronide prodrugs is reported and the potential of such SMEPT coatings against biofilm forming pathogens is evaluated. The fluoroquinolone glucuronide prodrugs exhibit excellent stability in absence of bioacatalytic coating and efficient enzymatic release in presence of biocatalytic coating as determined by analytical HPLC. The SMEPT coatings were assembled through layer-by-layer technique consisting of poly(sodium-styrene-sulfonate) and poly(allylamine hydrochloride), two non-degradable polymers ensuring long durability and stability of the coatings. The enzymatic trigger is effectively immobilized within the layers and remains stable within the course of treatment. MICs and MBCs of the biocatalytic coatings against various clinically relevant bacterial strains, such as Escherichia coli, Staphylococcus aureus and epidermidis, were evaluated. An exemplary dose-response curve of the biocatalytic surface coatings and fluoroquinolone glucuronide prodrugs against Escherichia coli is depicted in Figure 1, right. The presented results are a proof-of-concept study and highlight the potential of SMEPT in conjunction with fluoroquinolone glucuronide prodrugs as an alternative approach for antibacterial coatings on medical implants.

Student presentation 2

A Graphene Competitor: Synthesis and Properties of sp/sp^2 All-Carbon Macrocyclic Fragments

Martin Drøhse Kilde, Mogens Brøndsted Nielsen.

Department of Chemistry, University of Copenhagen, Universitetsparken 5, 2100 KBH Ø, Denmark.

martinkilde91@gmail.com, mbn@chem.ku.dk

Synthetic carbon allotropes are majestically eye pleasing architectures. They also possess outstanding materials properties with the fullerenes and carbon nanotubes being the big players. The characteristic conjugation of these molecules leads to well defined redox activity and electronic properties. (i) Recent years have led to the exploration of graphene as a new "wonder material", while theoreticians have found that sp/sp^2-hybrid carbon networks are far superior to graphene. (ii)

Here we will present the synthesis and properties of fragments of graphyne. The work includes a strategically sophisticated synthesis based on Pd-catalyzed chemistry and the properties of this series of all-carbon macrocyclic fragments inspired of 6,6,12-graphyne (Fig. 1).

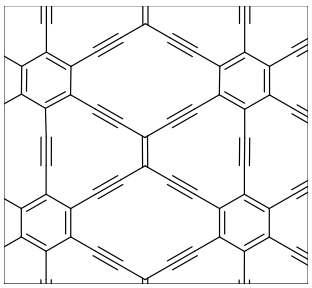


Figure 1: Schematic representation of a section of 6,6,12-graphyne.

i. A. Hirsch, *Nat. Mater.*, **2010**, 9, 868-871.
ii. M. Zhao, W. Dong, A. Wang, *Sci. Rep.*, **2013**, 3, 3532

Student presentation 3

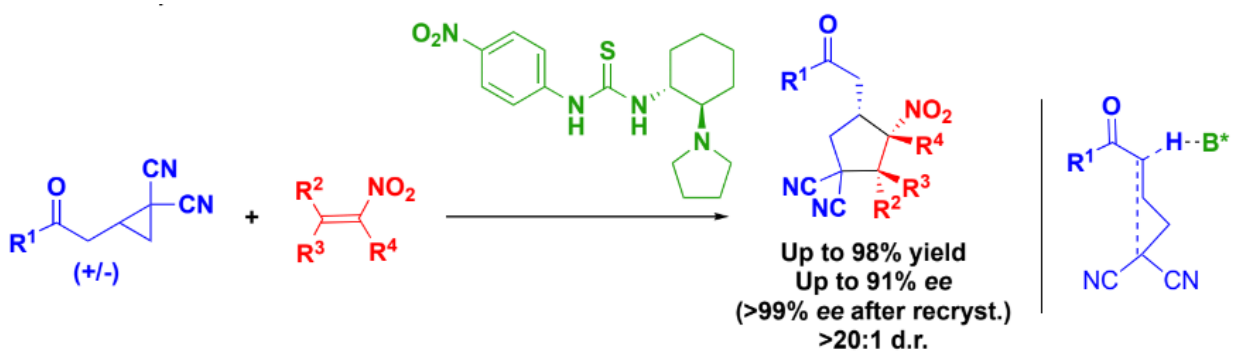
Directing the Activation of Donor-Acceptor Cyclopropanes Towards Stereoselective 1,3-Dipolar Cycloaddition Reactions by Brønsted Base Catalysis[1]

Jakob Blom and Karl Anker Jørgensen.

Department of Chemistry, Aarhus University, Langelandsgade 140, 8000 Aarhus C, Denmark. E-mail: Blom@chem.au.dk

Multiple stereocentered cyclopentanes are challenging to construct and as of such 1,3-dipole synthons in the form of donor-acceptor cyclopropanes have within the last decades gained increasing interest. Most of the attention has been centered on Lewis acid activation of donor-acceptor cyclopropanes and only very recently examples of stereoselective organocatalyzed systems have emerged.

The presentation describes the development of a novel organocatalytic activation mode for donor-acceptor cyclopropanes resulting in the first organocatalyzed stereoselective [3+2] cycloaddition reaction of donor-acceptor cyclopropanes. The stereoselective 1,3-dipolar reactivity of the donor-acceptor cyclopropanes is achieved by applying an optically active bifunctional Brønsted base catalyst.



It is demonstrated, that the activation of racemic di-cyano cyclopropyl-ketones in the presence of mono- and polysubstituted nitroolefins leads to highly substituted cyclopentanes with the formation of three consecutive stereocenters in up to 98% yield, 91% *ee* and with consistent >20:1 dr. Variations on both the donor-acceptor cyclopropane and the nitroolefin are tolerated and 21 representative examples of such are given.

The enantiomeric excess of the cycloaddition adducts can be enriched by recrystallizations and optically pure products can be obtained. To broaden the synthetic value of the developed methodology, it is demonstrated that chemoselective transformations on the cycloaddition adduct scaffold are possible.

[1] J. Blom, A. V.-Albalat, J. Jørgensen, C. L. Barløse, K. S. Jessen, M. V. Iversen, K. A. Jørgensen, *Angew. Chem. Int. Ed.* **2017**, *56*, 11831-11835.

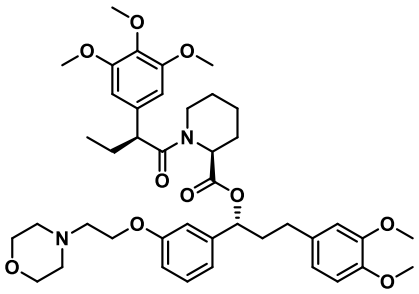
Student presentation 4

Efficient and enantioselective synthesis of Shield-1

Frederik Præstholm Jørgensen, Mikael Bols

Department of Chemistry, University of Copenhagen, Universitetsparken 5, 2100 København Ø, Denmark.
FPJ@chem.ku.dk bols@chem.ku.dk

The drug Rapamycin acts as an immunosuppressant via a mechanism that involves binding to FKBP12. Shield-1 is an analogue of Rapamycin that is capable of reversibly and selectively binding mutated forms of FKBP12, to stabilize and increase production of the proteins of interest.[1] This unique system represents an environmentally friendly alternative to the conventional methods of chemically modifying plants to increase crop yields used in agriculture today. In this project we wish to investigate derivatives of Shield-1 in plants in order to create compounds that can stimulate protein synthesis.



Shield-1

Here we present an optimized synthetic procedure for Shield-1 production and the syntheses of a series of novel analogues. Furthermore, we present the results of *in vivo* binding studies from these analogues.

[1] Banaszynski, L. A.: Chen, L-C.; Maynard-Smith, L. A.; Ooi, A. G. L.; Wandless, T. J., Cell **2006**, *126*, 995-1004.

Student presentation 5

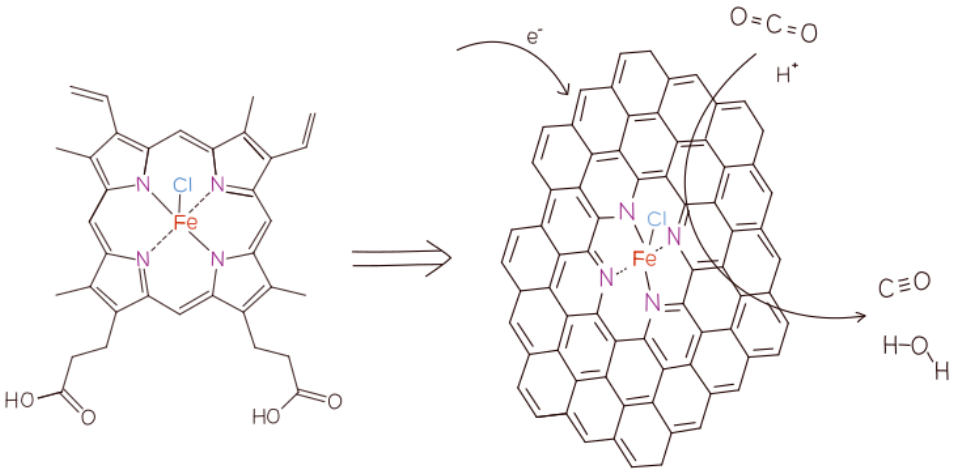
Green carbon materials for CO_2 electrochemical reduction

Matteo Miola, Kim Daasbjerg

Interdisciplinary nanoscience Centre (iNANO), Aarhus university, Gustav Wieds Vej 14, Aarhus, Denmark.
matteo.miola@inano.au.dk

Porphyrin-like structures in graphitic carbon scaffolds show high activity towards the electrochemical CO_2 conversion[1,2]. In collaboration with LIKAT (Leibniz institute of catalysis), earth abundant metals are combined with green and cheap nitrogen and carbon sources to produce porphyrin-like sites as catalysts for the CO_2 to CO electrochemical conversion. The catalysts are synthetized by pyrolysis at 800°C under inert atmosphere. In specific, hemin is an iron protoporphyrin that can be extracted from animal blood.

The hemin-based materials show outstanding catalytic activity, with high selectivity F.E.= 95-99 % and high current density J= 3.7 mA/cm^2.



1. A. S. Varela, N. Ranjbar Sahraie, J. Steinberg, W. Ju, H. S. Oh and P. Strasser, *Angew Chem Int Ed Engl*, 2015, 54, 10758-10762.

2. M.-J. Cheng, Y. Kwon, M. Head-Gordon and A. T. Bell, *The Journal of Physical Chemistry C*, 2015, 119, 21345-21352.

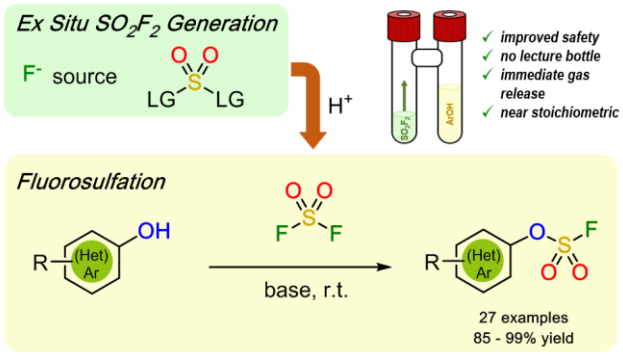
Student presentation 6

Ex Situ Generation of Sulfuryl Fluoride for the Synthesis of Aryl Fluorosulfates[1]

Cedrick Veryser, Joachim Demaerel, Vidmantas Bieliūnas, Philippe Gilles,
and Wim M. De Borggraeve.

Department of Chemistry, KU Leuven, Celestijnenlaan 200F, 3001 Leuven, Belgium. cedrick.veryser@kuleuven.be

Aryl fluorosulfates are useful starting materials in synthesis, either for their pseudohalide character or their ability to undergo the **SuFEx click reaction**[2]. Here, a convenient method for the transformation of phenols into the corresponding aryl fluorosulfates is presented. This comprises the first protocol which completely circumvents direct handling of gaseous sulfuryl fluoride (SO_2F_2) and its associated costs and dangers.



The proposed method employs **1,1'-sulfonyldiimidazole as a convenient precursor** to generate near stoichiometric amounts of SO_2F_2 gas using a **two-chamber reactor**[3]. With NMR studies, we were able to show that this *ex situ* gas evolution is extremely rapid, and a variety of phenols and hydroxylated heteroarenes were fluorosulfated in good to excellent yields. We propose this method as a pragmatic alternative for research labs without access to the corresponding gas bottle.

[1] C. Veryser, J. Demaerel, V. Bieliūnas, P. Gilles, W. M. De Borggraeve, *Org. Lett.,* **2017**, DOI: 10.1021/acs.orglett.7b02522

[2] J. Dong, L. Krasnova, M. G. Finn, K. B. Sharpless, *Angew. Chem. Int. Ed.,* **2014**, *53*, 9430-9448.

[3] S. D. Friis, A. T. Lindhardt, T. Skrydstrup, *Acc. Chem. Res.,* **2016**, *49*, 594-605.

Student presentation 7

SYNTHESIS OF ARABINOXYLAN FRAGMENTS

Emilie Nørmølle Underlin, Maximillian Felix Böhm, and Robert Madsen.

Department of Chemistry, Technical University of Denmark, Kemitorvet Bygn. 206, 2800 Kgs. Lyngby, Denmark. Email: emnu@kemi.dtu.dk

Dietary fibres or the indigestible parts of plant-derived food are considered anti-nutritional to e.g. swine and poultry due to their slow digestion. To enhance the availability of the nutrients a mixture of degrading enzymes can be added to the feed. The definition of dietary fibres covers hemicellulose, which is the second most abundant class of polysaccharides in the plant kingdom. Arabinoxylans (AX) is an important subclass of hemicellulose. However, in many instances, the biosynthesis and degradation remain elusive, hence synthetic AX fragments which can be submitted to enzymatic studies can improve our knowledge [1], [2].

The AX fragments have a backbone of β-1,4-linked xylans with α-L-arabinose units attached at specific positions. The synthesis utilises an efficient synthetic route, where all the xylan units derives from D-xylose through a common intermediate. The xylan units feature the same thiophenyl donor functionality to allow for successive coupling with the same optimised glycosylation protocol [3]. Then, attachment of the arabinose units and global deprotection yields the target AX fragments.

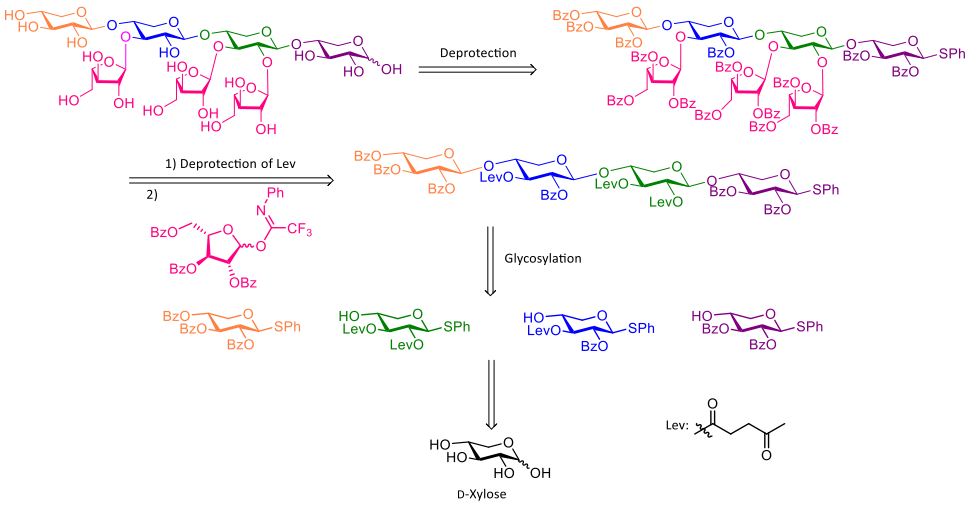


Figure 1: Retrosynthetic overview with one target as an example.

[1] J. Lindberg; *J. Anim. Sci. Biotech.*, **2014**, *5*, 15 [2] R. Jha; J. D. Berrocoso; *Animal*, **2015**, 9, 1441-1452 [3] D. Crich; F. Cai; F. Yang; *Carbohydr. Res.,* **2008**, *343*, 1858-1862

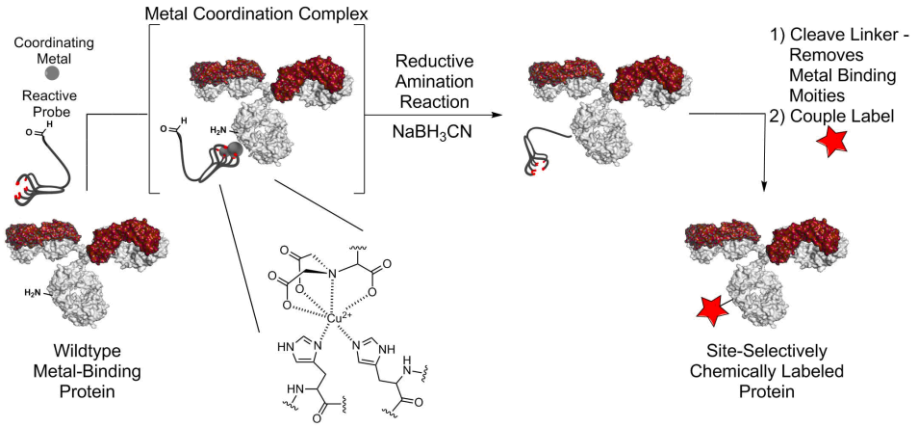
Student presentation 8

Metal-Mediated Site-Selective Antibody Labeling

Mikkel B. Skovsgaard, Michael R. Mortensen, Anders H. Okholm, Daniel M. Dupont, Thorbjørn B. Nielsen, Carsten Scavenius, Jan J. Enghild, Jørgen Kjems and Kurt V. Gothelf.

iNANO, Department of Chemistry, Aarhus University, Gustav Wieds vej 14, 8000 Aarhus, Denmark.
M.bach@inano.au.dk

Protein conjugates, and especially antibody conjugates, have a wide variety of applications both in medicine and biotechnology. However, the main challenge, when making protein conjugates, is to make homogenous products, securing uniform behavior. In our group, we have developed a method providing easy access to site-selectively modified metal-binding proteins without the need for genetic manipulation of the proteins. We utilize a small-molecule probe capable of forming a metal complex consisting of nitrilotriacetic acid (NTA) moieties on the small-molecule, a copper ion and metal-coordinating residues on the protein. This complex increases the local concentration of the reactive moiety at the protein surface, facilitating the conjugation. This strategy has allowed us to modify IgG1 antibodies in a site-selective manner using reductive amination.



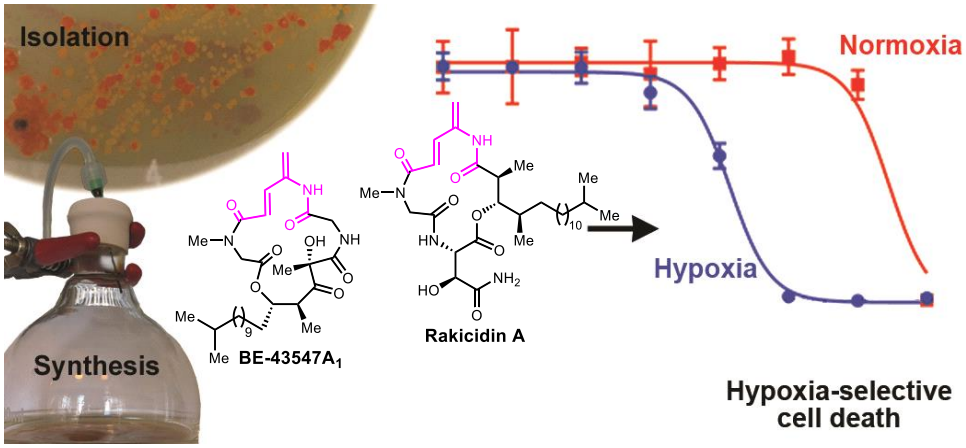
The labeling reaction using the small-molecule incorporates either an azide, for further modification via a click reaction, or a cleavable linker. The NTA groups are released from the protein conjugate upon cleavage of the linker, leaving a reactive handle on the protein. The reactive handle can be used for further modification of the protein with desired functionalities, such as fluorophores, DNA or drugs. Our strategy allows for purification of the conjugates, resulting in increased homogeneity. Furthermore, we have investigated the labeling sites and activity of the conjugates by several techniques showing labeling of a few lysine residues and retained affinity of the antibody conjugates.

Student presentation 9

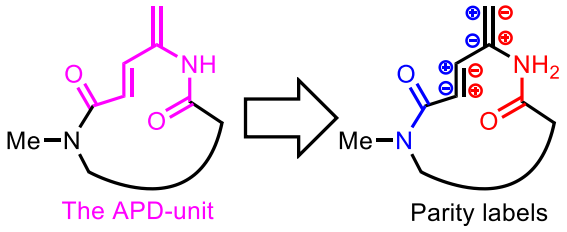
Chemistry and Biology of the APD-CLD Natural Product

Nikolaj L. Villadsen, Kristian M. Jacobsen, Per Hjerrild, Thomas Tørring, and Thomas B. Poulsen. Department of Chemistry, Aarhus University, Langelandsgade 140 Aarhus C, Denmark. nlv@chem.au.dk

The 4-amido-2,4-pentadienoate-containing cyclolipodepsipeptides (APD-CLD) are a group of natural products. Our interest in these molecules originates from their hypoxia-selective cytotoxicity towards human cancer cells, but the APD-unit also offer interesting unexplored territory from a synthetic and biosynthetic point of view. Primarily rakicidin A and BE-43547A$_1$ have been our focus, and we have published synthesis of both natural products.[1,2] We aim to synthesize a simplified analog of rakicidin A or BE-43547A$_1$ with improved properties to advance towards clinical studies.



The 4-amido-2,4-pentadienoate (APD)-unit defines the family of natural products, and their cytotoxicity is dependent on this functionality. Assignment of parity labels display a dissonant relationship of the APD-unit emphasizing the unpredictable reactivity. Understanding the APD-unit is key to understand and tune reactivity of natural product analogs.



[1] Villadsen, N. L., Jacobsen, K. M., Keiding, U. B., Weibel, E. T., Christiansen, B., Vosegaard, T., Bjerring, M., Jensen, F., Johannsen, M., Tørring, T. & Poulsen, T. B. Synthesis of *ent*-BE-43547A1 reveals a potent hypoxia-selective anticancer agent and uncovers the biosynthetic origin of the APD-CLD natural products. *Nat. Chem.* **9,** 264–272 (2017).

[2] Tsakos, M., Clement, L. L., Schaffert, E. S., Olsen, F. N., Rupiani, S., Djurhuus, R., Yu, W., Jacobsen, K. M., Villadsen, N. L. & Poulsen, T. B. Total synthesis and biological evaluation of rakicidin A and discovery of a simplified bioactive analogue. *Angew. Chem. Int. Ed.* **55,** 1030–1035 (2016).

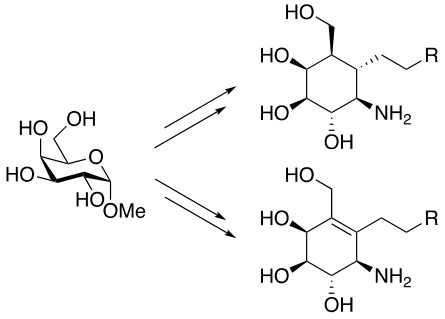
Poster 1

Towards the Synthesis of Potential Inhibitors for GALC

Linette Brøndum Iversen, Christinne Hedberg, Henrik H Jensen*.

Department of Chemistry, Aarhus University, Langelandsgade 140, 8000 Aarhus C, Denmark. linette@kubeligh.dk

In this project we aim to synthesize potential inhibitors for β-galactocerebrosidase (GALC) as chemical chaperones for the treatment of the autonome lysosomal storage disease, Krabbe disease. The inhibitors are synthesized from methyl-α-D-galactopyranoside and the design is inspired by the transition state of GALC catalyzed hydrolysis.



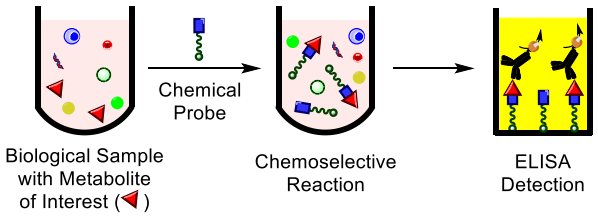
Poster 2

Quantification of Unstable Metabolites in Biological Samples

Rasmus Kold-Christensen, Ulrik B. Keiding, Troels R. Kjær, and Mogens Johannsen.

Department of Forensic Medicine, Aarhus University, Palle Juul-Jensens Boulevard 99, 8200 Aarhus N, Denmark.
rkc@forens.au.dk

Rapid quantification of unstable metabolites in biological samples is difficult using conventional methods. To solve this problem we have recently developed a novel type of enzyme-linked immunosorbent assay (ELISA) which utilizes a chemical probe that is able to react chemoselective with the metabolite of interest, thereby stabilizing it and allowing ELISA detection, a method we have termed ReactELISA.[1]



[1] E.F. Holmquist, U.B. Keiding, R. Kold-Christensen, T. Salomón, K.A. Jørgensen, P. Kristensen, T.B. Poulsen, M. Johannsen, *Anal. Chem.,* **2017**, *89 (9)*, 5066-5071.

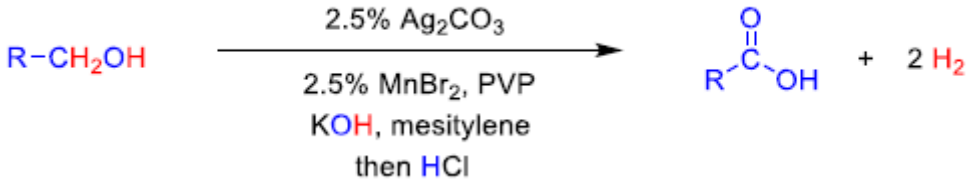
Poster 3

Silver-Catalyzed Dehydrogenative Synthesis of Carboxylic Acids from Primary Alcohols

Fabrizio Monda, Robert Madsen.

Department of Chemistry, Technical University of Denmark, 206, 2800 Kgs. Lyngby, Denmark.
fabm@kemi.dtu.dk

A simple silver-catalyzed protocol has been developed for the acceptorless dehydrogenation of primary alcohols into carboxylic acids and hydrogen gas. The procedure uses 2.5% Ag2CO3 and 2.5–3 equiv. of KOH in refluxing mesitylene to afford the potassium carboxylate which is then converted into the acid with HCl.[1] The reaction can be applied to a variety of benzylic and aliphatic primary alcohols with alkyl and ether substituents. The dehydrogenation is believed to be catalyzed by silver nanoparticles that are formed in situ under the reaction conditions.



[1] Golshadi, H.; Madsen, R. *Chem. Eur. J.* **2017**, *23*, 1–8.

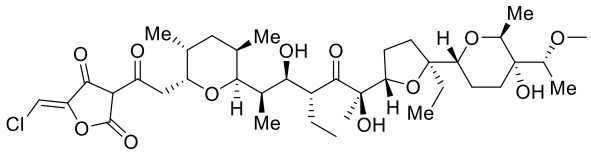
Poster 4

A semi-synthetic route towards nonthmicin

Christine Nøhr Pedersen, Shaoquan Lin, and Thomas B. Poulsen*.

Department of Chemistry, Aarhus University, Langelandsgade 140, 8000 Aarhus C, Denmark.
christine.n.pedersen@gmail.com

The objective of this project is to develop a semi-synthetic route towards non-natural analogs of the natural product nonthmicin (**1**). Nonthmicin is a new polyether ionophore which shows neuroprotective properties and selective antibacterial activity. Non-natural analogs are pursued by convergent coupling of complex, yet highly abundant, building blocks.



(1)

(1) Igarashi, Y.; Matsuoka, N.; In, Y.; Kataura, T.; Tashiro, E.; Saiki, I.; Sudoh, Y.; Duangmal, K.; Thamchaipenet, A. *Org. Lett.* **2017**, *19*, 1406.

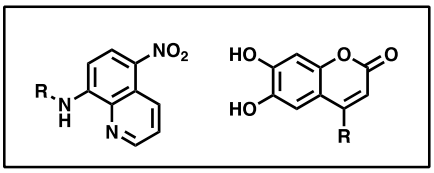
Poster 5

New drugs against chronic infections

Katia Elizabeth Thomsen and Katrine Qvortrup.

Chemistry department, Technical University of Denmark, Kemitorvet B206, 1000 University City, Denmark.
s134444@student.dtu.dk

Chronic infections are often caused by bacterial biofilms. Biofilm infections typically develop on implants and medical equipment or associated with distinct disease states. In addition, recent intensive research on human microbiomes and their impact on health and disease provide emerging evidence that certain cancers may be promoted by bacterial biofilms. Bacteria in biofilms attain the highest levels of resistance to the current antibiotics, and almost unlimited capacity to evade host immunity. In this project we are synthesizing compounds with biofilm dispersal activity. The aim is to develop the first composite drug - i.e. one molecule seeking two antimicrobial targets (biofilm dispersal and killing of planktonic bacteria), with the full eradication of infective bacteria as an endpoint.



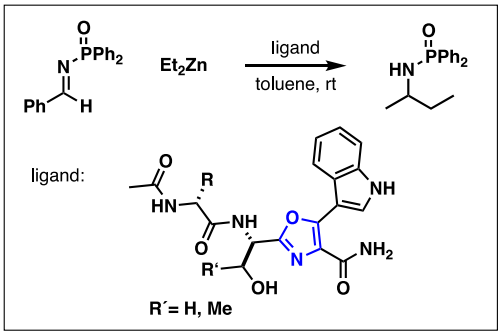
Poster 6

Oxazole-containing peptidic structures as ligands in asymmetric synthesis

Mathias Thor Nielsen and Katrine Qvortrup.

Chemistry department, Technical University of Denmark, Kemitorvet B206, 2800 Lyngby, Denmark
s134469@student.dtu.dk

We recently developed a route allowing for solid-phase oxidative cyclization of small peptides containing tryptophan, *unpublished*. In this project, we employ this strategy to synthesize a combinatorial library of indolyl-oxazole containing chiral ligands. Chirality is introduced by the use of cheap natural amino acids. Hereby, we identify ligands allowing for enantioselective addition of $ZnEt_2$ to imines.



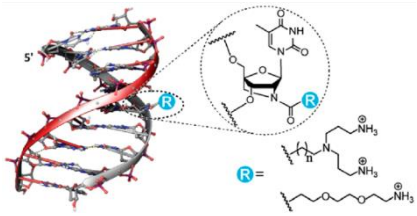
Poster 7

Oligonucleotides Containing Aminated 2'-Amino-LNA Nucleotides:

Simone V. Samuelsen, Chenguang Lou, Jesper Wengel.

DTU Chemistry, Technical University of Denmark, Anker Engelunds Vej 1, 2800 Kgs. Lyngby, Denmark.
ssam@kemi.dtu.dk

Mono- and diaminated 2'-amino-LNA monomers were synthesized and introduced into oligonucleotides. Each modification imparts significant stabilization of nucleic acid duplexes and triplexes, excellent sequence selectivity and significant nuclease resistance. Molecular modeling suggested that structural stabilization occurs via intrastrand electrostatic attraction between the protonated amino groups of the aminated 2'-amino-LNA monomers and the host oligonucleotide backbone.[1]



[1] Chenguang, L.; Samuelsen, S. V.; Christensen, N. J.; Vester, B.; Wengel, J.; *Bioconjugate Chem*, **2017**, *28*, 1214-1220

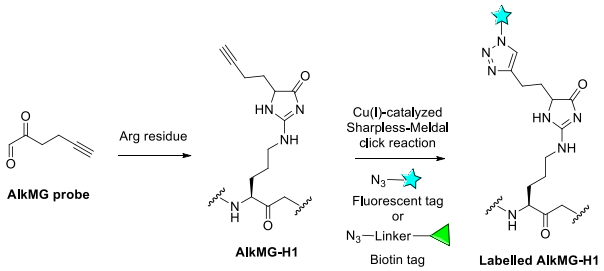
Poster 8

Concomitant Probe-Based Profiling of Methylglyoxal Blood Metabolism and Post-translation Modification

A.S. Oxvig[1], C. Sibbersen,[1] J. Palmfeldt,[2] K.A. Jørgensen[3] and M. Johannsen[1]

[1]Department of Forensic Medicine, [2]Department of Clinical Medicine, [3]Department of Chemistry, AU,
annemette.oxvig@forens.au.dk

Methylglyoxal, a glycolytic byproduct, is known to post-translationally modify proteins and to be implicated in aging and diabetes related pathologies. With the use of small-molecule probes and click chemistry, we have developed a generic protocol to study the metabolism of endogenous compounds such as methylglyoxal in parallel with the formation of their adducts with proteins in biological samples.



Poster 9

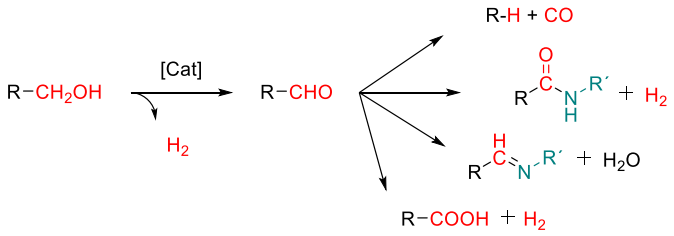
METAL-CATALYZED ACCEPTORLESS ALCOHOL DEHYDROGENATION

Fabrizio Bottaro and Robert Madsen

DTU Chemistry, Technical University of Denmark, Anker Engelunds Vej 1, 2800 Lyngby, Denmark. fabo@kemi.dtu.dk

Acceptorless alcohol dehydrogenation has been gaining attention in several applications, such as hydrogen production from biomass,[1] despite that the high cost of precious metal catalysts limits its exploitation.

The purpose of this project is to develop cheap and simple *in situ* formed metal catalysts for releasing hydrogen gas from primary alcohols and obtaining valuable products from the corresponding aldehydes.



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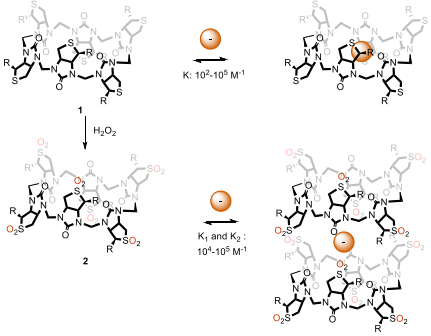
Poster 10

Biotinsulfone[6]uril: anion receptors showing two-to-one binding stoichiometries in water

Andersen, Nicolaj Nylandsted, Eriksen, Kristina, Lisbjerg, Micke, Ottosen, Mille, Akselsen, Olivia Mulvad and Pittelkow, Michael

Department of Chemistry, University of Copenhagen, Denmark

By oxidation of the previously reported biotin[6]uril **1**,[1] biotinsulfone[6]uril **2** is obtained. Whereas the biotin[6]uril exhibits one-to-one recognition of anions in both aqueous[2] and organic[3] media employing twelve CH-X interactions, the biotinsulfone[6]uril shows two hosts to one guest stoichiometries. The binding affinity of parent biotin[6]uril ranges from 10^2 m^{-1} for smaller anions to 10^5 m^{-1} for larger anions. Biotinsulfone[6]uril, however, more consistently recognises anions in the 10^4 to 10^5 m^{-1} regime with no apparent preference for size.



[1] M. Lisberg *et al*. Chem. Sci., **2014**, 5 (7), 2647-2650.

[2] M. Lisberg *et al*. Org. Biomol. Chem., **2015**, 13, 369-373.

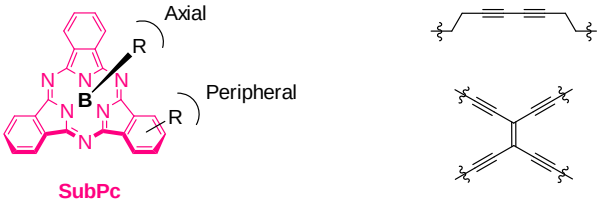
[3] M. Lisberg *et al*. J. Am. Chem. Soc., **2015**, 137(15), 4948-4951.

Poster 11

Methodologies for Synthesis of Dimeric Structures Containing Subphthalocyanine Chromophores

Line Broløs, Mogens Brøndsted Nielsen *et al*., Department of Chemistry, University of Copenhagen, Universitetsparken 5, 2100 Copenhagen, Denmark. Fqd896@alumni.ku.dk

Boron subphthalocyanines (SubPcs) are powerful chromophoric heterocycles that pose as interesting candidates in the development of dye sensitized solar cells.[1] The connection of SubPc to acetylenic scaffolds offers a way of preparing remarkable architectures. Here we present synthetic methodologies for functionalizing the SubPc chromophore via acetylenic reactions, and compare the properties of novel dimeric structures.[2]



[1] C. G. Claessens, D. Gonzáles-Rodríguez, M. S. Rodríguez-Morgade, A. Medina, T. Torres, *Chem. Rev.* **2014**, 114, 2192-2277.

[2] H. Gotfredsen, L. Broløs, M. B. Nielsen *et al*., *Org. Biomol. Chem.* (In Press)

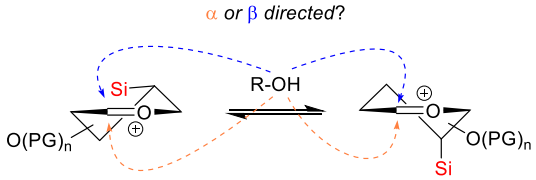
Poster 12

TAMING THE REACTIVITY OF C-SILYLATED GLYCOSYL DONORS

Martin Jæger Pedersen, Christian Marcus Pedersen*

Department of Chemistry, University of Copenhagen, Universitetsparken 5, 2100 Copenhagen Ø, Denmark. e-mail: cmp@chem.ku.dk

Protecting groups provide a range of inductive, steric torsion and direct partition effects during glycosylation,[1] while commonly preserving the parent oxygen- or nitrogen-group on the furan- or pyranoside ring-system. We explored, how having silicium directly onto a ring-system affected the selectivity of glycosylations, as reactivity increased by inductive effects, β stabilization[2] or longer bond lenght.[3]



[1] J. Guo, X.-S. Ye, *Molecules* **2010**, *15*, 7235–7265.
[2] F. C. Whitmore, L. H. Sommer, *J. Am. Chem. Soc.* **1946**, *68*, 481–484.
[3] R. A. Ballinger, N. H. March, *Nature* **1954**, *174*, 179.

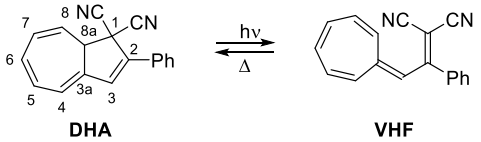
Poster 13

OPTIMIZATION OF THE DIHYDROAZULENE-VINYLHEPTAFULVENE SYSTEM

Josefine Mogensen, Dianna Andersen, Martin Drøhse Kilde, Mogens Brøndsted Nielsen.

Department of Chemistry, University of Copenhagen, Universitetsparken 5, 2100 København Ø, Denmark.
mbn@chem.ku.dk

Dihydroazulene (DHA) undergoes upon irradiation with light an isomerization to the metastable vinylheptafulvene (VHF). [1] Here we present two new structure modulations. Firstly, attaching EWG's directly on the seven-membered ring showed remarkable photophysical property changes compared to the parent DHA-VHF system. Secondly, substituting one of the cyanogroups on C1 with different substituted benzothiazoles showed a linear correlation between the rate of back-reaction (VHF → DHA) and the electronic properties of the substituents on the benzothiazole-derivatives.



[1] S. L. Broman, M. B. Nielsen, *Phys. Chem. Chem. Phys.,* **2014**, *16*, 21172-21182.

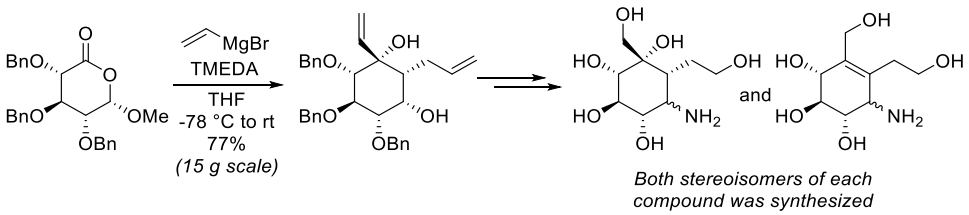
Poster 14

INVESTIGATION OF A NOVEL FERRIER-TYPE CARBOCYCLIZATION AND ITS USE IN GLYCOSIDASE INHIBITOR SYNTHESIS

Christinne Hedberg, Ida M. B. Knudsen, Morten Estrup, Anne Brinkø, Espen Z. Eikeland and Henrik H. Jensen.

Department of Chemistry, Aarhus University, Langelandsgade 140, 8000 Aarhus C, Denmark. chedberg@chem.au.dk

A novel Ferrier-type carbocyclization is reported. It involves a carbohydrate-derived lactone acetal, which upon treatment with excess vinylmagnesium bromide stereoselectively provided a highly substituted carbocyclic product. A possible reaction mechanism has been proposed and the reaction has been used in the synthesis of new potential glycosidase inhibitors.



Poster 15

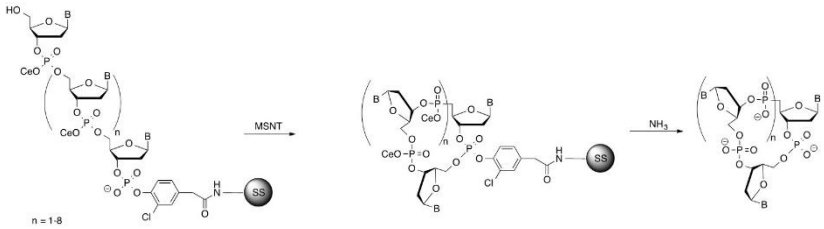
Small Cyclic Oligonucleotides

Alexander Sandahl, Kurt Gothelf.

iNANO, Aarhus University, Gustav Wieds Vej 14, 8000 Aarhus, Denmark.

Asandahl@inano.au.dk

Nature produces a large amount of oligomers and polymers based on a few set of building blocks i.e. saccharides, amino acids and nucleotides. The oligomers are well known in their linear forms, however only cyclic forms have been discovered for oligosaccharides (e.g. cyclodextrins) and oligopeptides and thereby not for oligonucleotides. The goal of this project is to synthesize small cyclic oligonucleotides and test them for biological activity in order to elucidate their biological context.



Poster 16

Molecular Adhesion Layers for Silicone Bonding

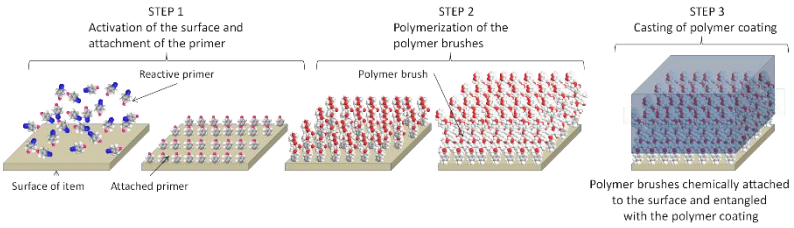
Stefan Urth Nielsen, Steen Uttrup Pedersen, Kim Daasbjerg and Mikkel Skorkjær Kongsfelt.

iNANO, Aarhus University, Gustav Wieds Vej 14, 8000 Aarhus C, Denmark.

RadiSurf ApS, Arresøvej 5B, 8240 Risskov, Denmark

Stefan-urth@inano.au.dk

In this work, the formation of polymer brushes (PB) that can mix and covalently bond to silicon is reported. Active groups are incorporated into the PB to enable strong interaction with the curing silicone. The tensile strength between the PB and silicone is evaluated and compared against commercial products.



Poster 17

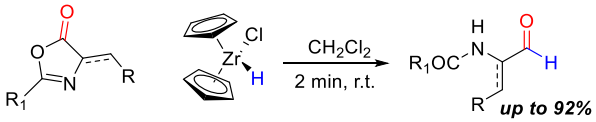
Chemoselective Reduction of Azlactones Using Schwartz's Reagent

Danielle L. J. P., Eloah P. A., Gabriel M. F. B., and Giovanni W. A.

Chemistry Department, Federal University of Juiz de Fora, Cidade Universitária, São Pedro, Juiz de Fora, MG CEP 36036-900, Brazil

dane_jf@hotmail.com

A highly chemoselective synthesis towards challenging α-amino aldehydes is presented. The developed methodology consists of the addition of Schwartz's reagent to azlactones and furnishes the desired product in good to excellent yields. The presence of sensitive functionalities or electronic factors does not compromise the potential of the method. Moreover, the α-amino aldehydes could be converted into highly functionalized allylic alcohol by using an excess of the reducing agent.[1]



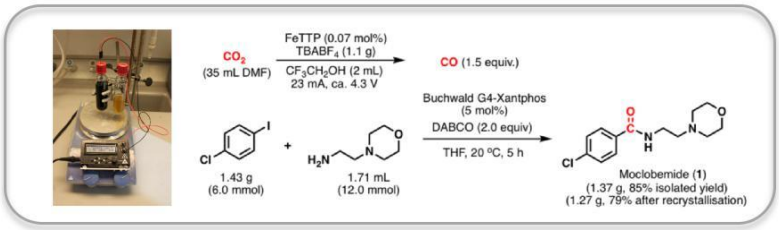
[1] D. L. J. Pinheiro, E. P. Ávila, G. M. F. Batista, G. W. Amarante, J. Org. Chem. **2017**, *82*, 5981−5985.

Poster 18

Scalable carbon dioxide reduction coupled to carbonylation chemistry

Anne K. Ravn*, Magnus H. Rønne*, Mikkel T. Jensen*, René W. Juhl, Dennis U. Nielsen, Xin--Ming Hu, Steen U. Pedersen, Kim Daasbjerg and Troels Skrydstrup. INANO, Aarhus University, Gustav Wieds Vej 14, 8000 Aarhus, Denmark. akr@inano.au.dk

Here we describe the design and application of a both inexpensive and user-- friendly electrochemical set--up combined with Pd-catalysed carbonylation reactions with near stoichiometric carbon monoxide. This combined two-- reaction process allows for milligram to gram synthesis of pharmaceutically relevant compounds. Moreover, this technology can be adapted to the use of atmospheric carbon dioxide.

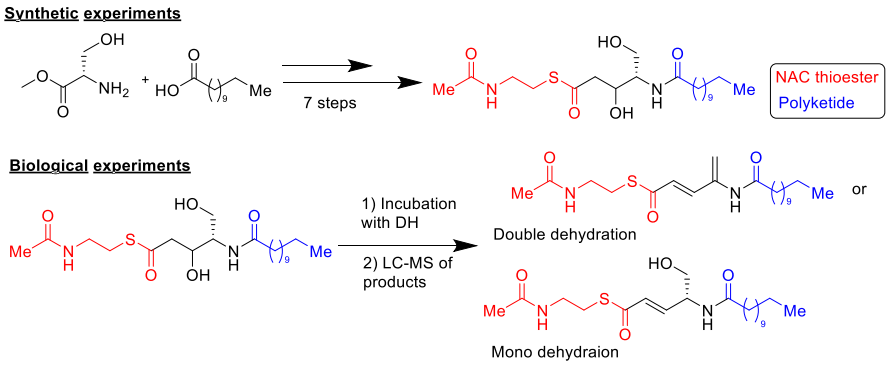


Poster 19

NAC thioester probes - chemical tools of biology

Freja Karlsen, zagandi1990@gmail.com ,Aarhus University, Department of chemistry, Group: Chemical biology

In our research, we aim to synthesize an N-acetylcysteamine (NAC) thioester. This thioester will subsequently be used as a chemical probe to study the biosynthesis of the APD group of the anticancer agent Rakicidin A. The APD group has proven to be indispensable to the cytotoxicity of Rakicidin A. We will use the probe to examine, if a single dehydratase (DH) domain makes a double dehydration in the formation of the APD group.



Poster 20

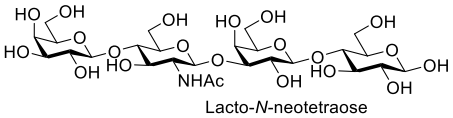
Human Milk Oligosaccharides

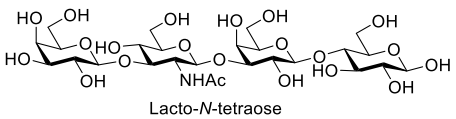
Helle H. Trinderup, Søren B. Prisak, Henrik H. Jensen.

Department of Chemistry, Aarhus University, Langelandsgade 140, 8000 Aarhus C, Denmark.

201407806@post.au.dk

The human milk oligosaccharides, Lacto-*N*-neotetraose and Lacto-*N*-tetraose, are thought to be beneficial for nursing infants. The aim is to synthesize Lacto-*N*-neotetraose and Lacto-*N*-tetraose using β-acyl *N*-acetyl lactoseamine and using β-acyl lacto-*N*-biose as donors and lactose as acceptor.





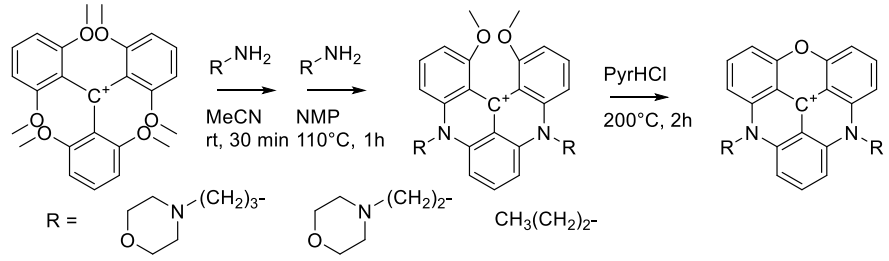
Poster 21

Synthesis of morpholino-substituted DAOTA$^+$-dyes for identification of G-quadruplex DNA in live cells by FLIM

Niels Bisballe, Marco Santella and Bo Wegge Laursen.

Department of Chemistry, University of Copenhagen, Universitetsparken 5, 2100 Copenhagen Ø, Denmark.
niels.bisballe@chem.ku.dk

A series of DAOTA$^+$-dyes functionalized with morpholino-substituents with varying linker lengths have been synthesized by S_NAr. The goal is to achieve a significant change in fluorescent properties for the dyes, depending on which higher order structure of DNA they bind to. A dye of this series has previously been synthesized, which by binding to G-quadruplex DNA shows distinct enhancement in emission.[1]



[1] Shivalingam, A. et al. *Nat Commun* **2015**, *6*.

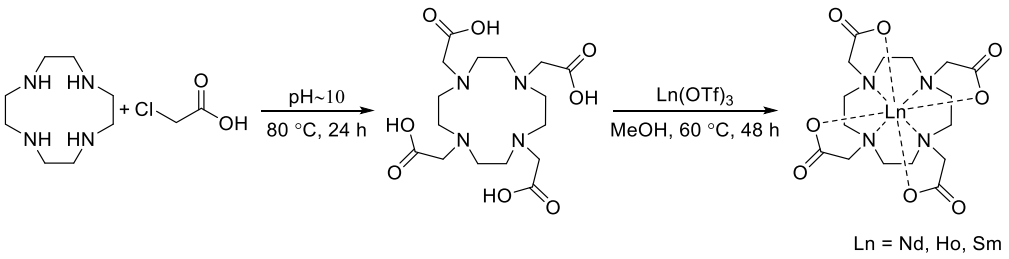
Poster 22

A STUDY OF MACROCYCLIC DOTA LANTHANIDE COMPLEXES

Helene Obel Bøch Andersen*, Loyan Salah, Charlotte Nybro Bjerking, Thomas Just Sørensen.

Department of Chemistry, University of Copenhagen, Universitetsparken 5, 2100 København Ø, Denmark.
tlj217@alumni.ku.dk

Kinetically inert lanthanide complexes are used as contrast agents in magnetic resonance imaging (MRI). Here we present the synthesis and photophysical properties of a series of 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) lanthanide complexes, as well as a structural investigation using paramagnetic NMR spectroscopy.[1,2]



[1] J. F. Desreux, Inorg. Chem., **1980**, *19*, 1319-1324.

[2] A. K. R. Junker, M Tropiano, S. Faulkner, T. J. Sørensen, Inorg. Chem., **2016**, *55,* 12299-12308.

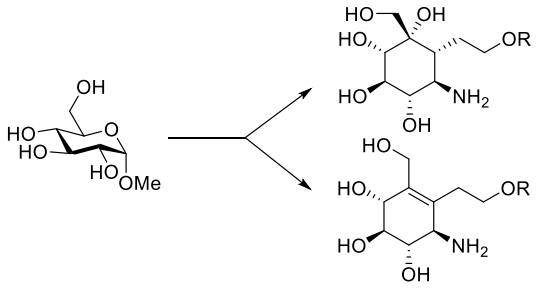
Poster 23

Towards the synthesis of potential inhibitors of GCase

Josefine H. Jakobsen and Henrik H. Jensen.

Department of Chemistry, Aarhus University, Langelandsgade 140, 8000 Aarhus C, Denmark. 201304023@post.au.dk

The aim of this project is to convert methyl α-D-glucopyranoside into two new types of potential inhibitors of the enzyme β-glucocerebrosidase (GCase) as potential pharmaceutical chaperones for treatment of Gaucher disease. The structures of the potential inhibitors are inspired by analogous natural products.



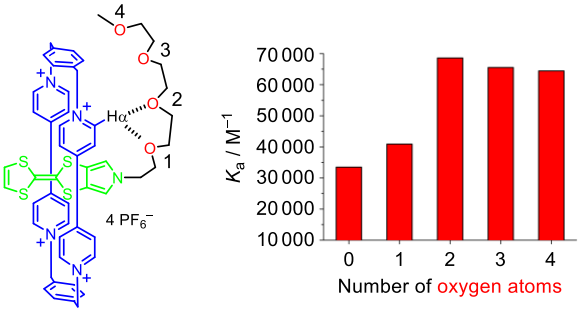
Poster 24

Probing the Role of Glycol Chain Lengths in π-Donor-Acceptor [2]Pseudorotaxanes Based on Monopyrrolo-Tetrathiafulvalene and Cyclobis(paraquat-*p*-phenylene)

Rikke Kristensen, Sissel S. Andersen, Gunnar Olsen, and Jan O. Jeppesen.

Department of Physics, Chemistry and Pharmacy, University of Southern Denmark, Campusvej 55, 5230 Odense M, Denmark. rikkek@sdu.dk

A homologous series of *N*-substituted monopyrrolo-tetrathiafulvalenes (MPTTF), were synthesized. These formed [2]pseudorotaxanes upon mixing with cyclobis-(paraquat-*p*-phenylene) ($CBPQT^{4+}$) and investigations found that increasing the number of oxygens from one to two increased the binding energy affiliated with the complexation between **1**–**5** and $CBPQT^{4+}$, whereas further increment of the number of oxygens did not increase the binding energy further. [1]



[1] Kristensen, R.; Andersen, S. S.; Olsen, G.; Jeppesen, J. O., *J. Org. Chem.,* **2017,** *82*, 1371-1379.

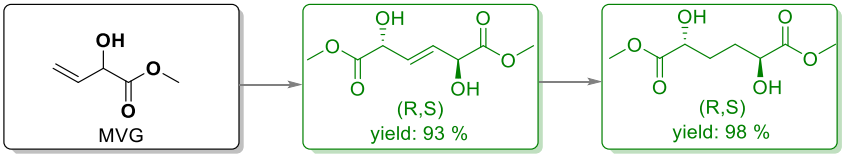
Poster 25

Development of Catalytic Reactions to Prepare Bio-Based Polymer Building Blocks.

B. M. Jessen,[1] A. B. Sølvhøj,[2] E. Taarning[2] and R. Madsen.[1]

[1]Technical University of Denmark, Department of Chemistry, 2800 Kgs. Lyngby Denmark, [2]Haldor Topsøe A/S, New Business R&D, 2800 Kgs. Lyngby, Denmark.
bojes@kemi.dtu.dk

The demand for bioplastics and new bio-renewable platform chemicals are expected to increase steadily in demand. However it is still difficult to compete with oil derived chemicals. We present new chemicals synthesized from the platform molecule Methyl Vinyl Glycolate (MVG) which is derived from a bio-renewable source.[1] Furthermore we are trying to find uses for these new chemicals. Polymerization is one application being tried.



[1] A. Sølvhøj, E. Taarning and R. Madsen, Methyl Vinyl Glycolate as a Diverse Platform Molecule, *Green. Chem,* 2016, **18**, 5448.

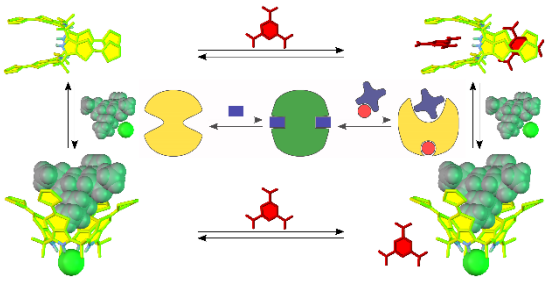
Poster 26

Tetrathiafulvalene-calix[4]pyrrole: A Biomimetic Sensor for Electron Deficient Spherical and Planar Guests

Steffen Bähring,[a,b] Jan O. Jeppesen,[a] and Jonathan L. Sessler[b]

[a]Department of Physics, Chemistry, and Pharmacy, University of Southern Denmark
[b]Department of Chemistry, The University of Texas at Austin
sbahring@sdu.dk

Tetrakis-tetrathiafulvalene-calix[4]pyrrole receptor has shown a remarkable diversity in complexation modes ranging from binding of ion pairs, spherical fullerenes and electron-deficient aromatic planar guests displaying cooperative binding, allosteric modulation by both agonists and antagonists leading to controlled electron-transfer processes. This has benchmarked the receptor as the smallest complex synthetic receptor.



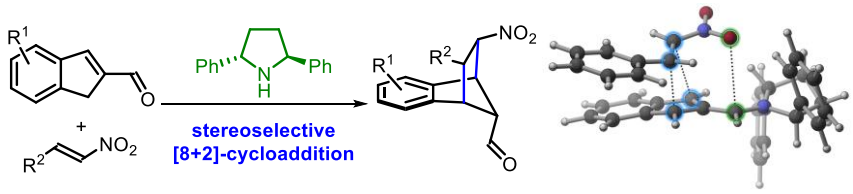
Poster 27

Organocatalytic Enantioselective Higher-Order Cycloadditions of *in situ* Generated Amino Isobenzofulvenes

Teresa A. Palazzo, Bjarke S. Donslund, Alicia Monleón, Mette Louise Christensen, Anne Dahlgaard, Jeremy D. Erickson, and Karl Anker Jørgensen.

Department of Chemistry, Aarhus University, Langelandsgade 140, 8000 Aarhus C, Denmark
tapalazzo@chem.au.dk

The [8+2]-cycloaddition of indene-2-carbaldehydes and nitro olefins is described to provide benzonorbornene scaffolds in a highly peri-, diastereo- and enantioselective fashion in the presence of a C_2-symmetric aminocatalyst. DFT calculations suggest a kinetically controlled, stepwise mechanism in which the stereochemistry is determined in the first bond forming event. Beyond the fruitful [8+2]-cycloadducts, [10+4]-cycloadducts have been identified *in silico* as potential off-pathway intermediates.



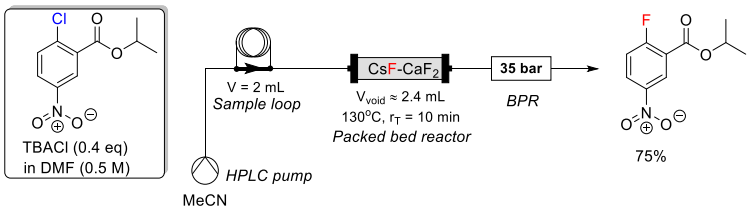
Poster 28

Calcium Fluoride as Ideal Solid Support for Nucleophilic Fluoride in Packed Bed Reactors

Martin B. Johansen, Anders T. Lindhardt.

Department of Engineering, Aarhus University, Hangøvej 2, 8200 Aarhus N, Denmark. bundgaard@eng.au.dk

A continuous flow set-up with a PBR containing CsF impregnated onto CaF_2 was adopted for nucleophilic benzylic and (hetero)aromatic fluorination reactions. CaF_2 was found to be the crucial as the ideal inert solid support in order to obtain reactive CsF in the PBR. Only 2 equivalents of CsF were needed as approximately half of the CsF was accessible in the packed bed column. Furthermore, catalytic amounts of CsF was proven efficient for the activation of TMS-CF_3 in trifluoromethylation of carbonyls.

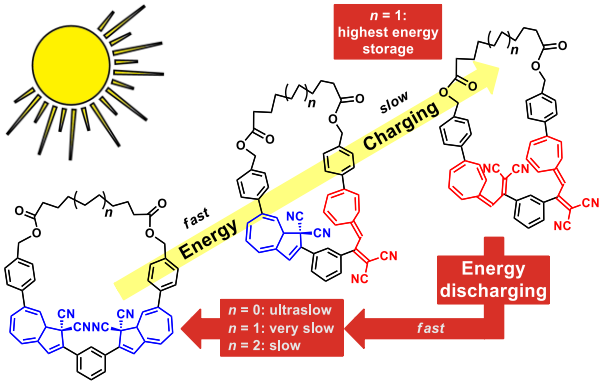


Poster 29

Macrocyclic DHA/VHF Systems Towards Molecular Solar-Thermal Energy Storage

Alexandru Vlasceanu, Benjamin N. Frandsen, Mads Koerstz Madsen, Anders B. Skov, Anne Schou Hansen, Henrik G. Kjaergaard, Kurt V. Mikkelsen, Mogens Brøndsted Nielsen*.

Department of Chemistry, University of Copenhagen, Universitetsparken 5, 2100 Copenhagen, Denmark. alexandru@chem.ku.dk



[1] A. Vlasceanu, B. N. Frandsen, A. B. Skov, A. S. Hansen, M. G. Rasmussen, H. G. Kjaergaard, K. V. Mikkelsen, M. B. Nielsen, DOI: 10.1021/acs.joc.7b01760

Poster 30

Lipidated Nucleic Acids as Tools for Programmable Fusion of Liposomes

Alexander Rabe, Philipp M. G. Löffler, Oliver Ries and Stefan Vogel.

Department of Physics, Chemistry and Pharmacy, University of Southern Denmark, Campusvej 55, 5230 Odense M, Denmark. rabe@sdu.dk

Artificial fusion systems has been used to study natural fusion processes, but also for drug delivery purposes or for the application of liposomes as nanoreactors. We present a programmable cascade of liposome fusion with efficient content mixing and low leakage, mediated by lipidated nucleic acids (DNA and peptide nucleic acids (PNA), Figure 1).[1]

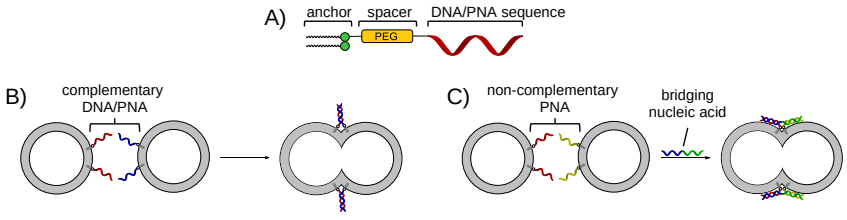


Figure 2. A) Design of a lipidated nucleic acid strand. B) Zipper fusion design. C) Double-zipper fusion design.

[1] P. M. G. Löffler, O. Ries, A. Rabe, A. H. Okholm, R. P. Thomsen, J. Kjems, S. Vogel, *Angew. Chem., Int. Ed.* **2017**, doi.: 10.1002/anie.201703243.

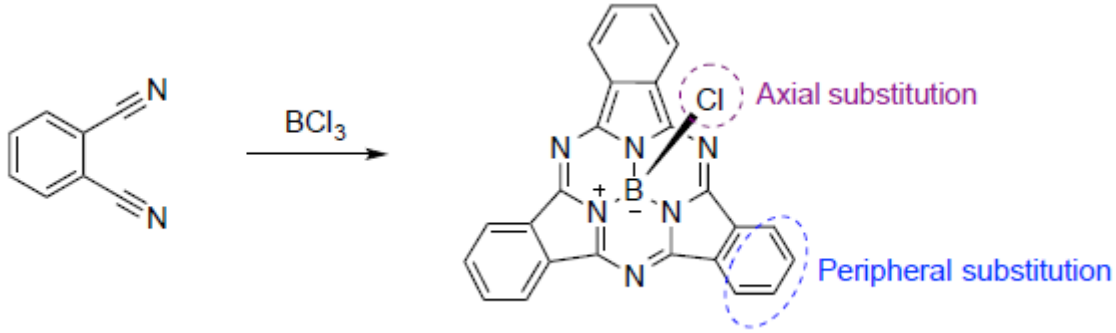
Poster 31

Subphthalocyanine scaffolds

Henriette Lissau and Mogens Brøndsted Nielsen.

Department of Chemistry, University of Copenhagen, Universitetsparken 5, 2100 København Ø, Denmark. lissau@chem.ku.dk

The boron(III) subphthalocyanine dye has been investigated for various purposes due to its light absorption properties in the visible range. The central focus of our synthetic work has been the introduction of halogens at the subphthalocyanine periphery followed by acetylenic coupling reactions to provide new acetylenic scaffolds. We aim at employing these as building blocks for construction of larger macrocyclic structures.



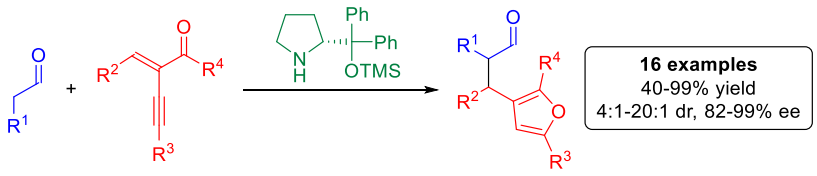
Poster 32

Metal-free Activation of Alkynes for the Asymmetric Synthesis of Chiral Furan Derivatives by Synergistic Amino and Brønsted Acid Catalysis

Danny K. B. Jørgensen and Karl Anker Jørgensen.

Department of Chemistry, Aarhus University, 8000 Aarhus, Denmark.

Furans are present in many natural products. The reaction presents a stereoselective construction of chiral furan derivatives by metal-free activation of alkynes. The reaction allows for highly functionalized products, and the concept can be extended to α,β-unsaturated aldehydes.



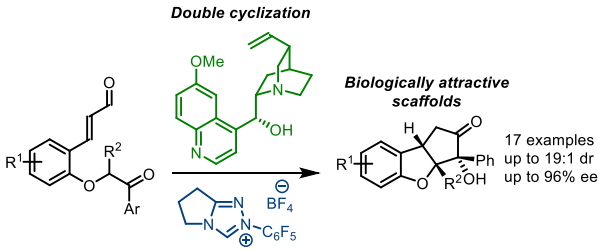
Poster 33

Enantioselective Synthesis of Cyclopenta[*b*]benzofurans via an Organocatalytic Intramolecular Double Cyclization

Bruno Matos Paz, Yang Li, Mathias Kirk Thøgersen and Karl Anker Jorgensen

Department of Chemistry, Aarhus University, DK-8000 Aarhus C, Denmark; kaj@chem.au.dk.

A concise construction of the privileged cyclopenta[*b*]benzofuran scaffold, present in many natural products with interesting biological activities, is demonstrated. The novel organocatalytic strategy relies upon an enantioselective double cyclization afforded by an unprecedented combination of Brønsted base catalysis and NHC catalysis. Cyclopenta[*b*]benzofurans were obtained in moderate to good yields and with excellent stereoselectivities.[1]



[1] B. M. Paz, Y. Li, M. K. Thøgersen, K. A. Jørgensen, *Chem. Sci,* **2017**, Accepted Manuscript; DOI: 10.1039/C7SC03006A

Poster 34

Post-Modification of Polymer Brushes for Molecular Adhesives

Kristian Birk Buhl[1], Andreas Nygaard Kolding[1], Steen Uttrup Pedersen[1], and Kim Daasbjerg[1]

[1]*Department of Chemistry and Interdisciplinary Nanoscience Center (iNANO), Aarhus University,*

Langelandsgade 140, DK-8000 Aarhus C, Denmark.
kbb@inano.au.dk

Abstract. Within surface modifications, nanometer thin polymer brushes are used to alter the properties of a material. Using the grafting from method via surface initiated atom transfer radical polymerization (SI-ATRP), polymer brushes with high grafting densities are obtained. The polymer brushes interact with bulk materials under the right conditions and provide high adhesive strength. To design polymer brushes with specific functionalities poly(glycidyl methacrylate) (PGMA) is a versatile platform to alter the reactivity and molecular affinity[1].

[1] M. Lillethorup, K. Shimizu, N. Plumere, S. U. Pedersen, K. Daasbjerg *Macromolecules* 47 (2014) 5081-5088.

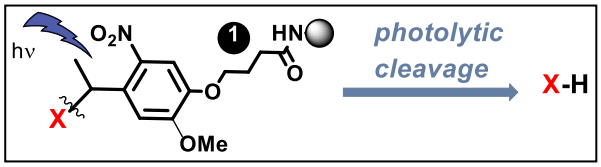
Poster 35

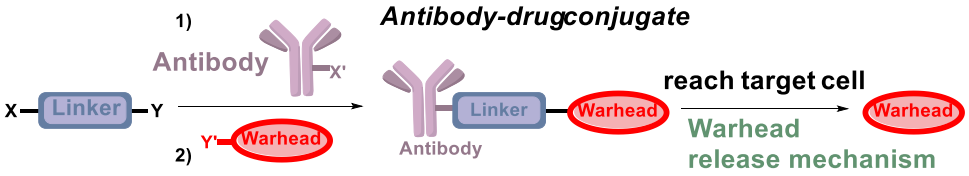
A Photolabile Linker for ADCs

Katja Egeskov Grier, Supervisor Katrine Qvortup

Department of Chemistry, Technical University of Denmark, Anker Engelundsvej 1, Lyngby
S134481@student.dtu.dk

Building on previous work[1] we will develop a photolabile linker to use in ADCs. The linker system displays high chemical stability and should offer the benefit of clean, remote- and dose controllable warhead release. Similar photo-linkers have also been used in biological applications for targeted cancer treatment at NIR[2].





[1] **K. Qvortup**, et. al., *Org. Lett.*, **2017**, **K. Qvortrup**, et. al., *Ang. Chem. Int. Ed*, **2016**
[2] *Mol. Pharmaceutics* **2016**, *13*, 1508 −1519

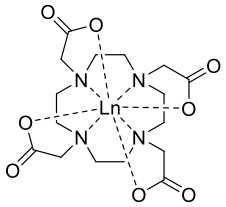
Poster 36

Examining solution structure of Ln(III) complexes with DOTA and DO3A

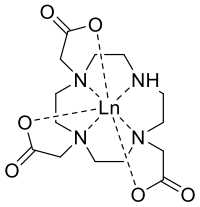
Lea Gundorff Nielsen and Thomas Just Sørensen.

Department of Chemistry, NanoScience Center, University of Copenhagen, Universitetsparken 5, 2100 Copenhagen Ø, Denmark, lea@science.ku.dk

Kinetically inert lanthanide(III) complexes are important in applications such as magnetic resonance imaging and bioassays.[1] Here, the coordination of thermodynamically stable ligands to a lanthanide metal centre have been investigated with paramagnetic NMR and luminescence. This has been done to establish the solution structure of complexes with DOTA and DO3A. Diamagnetic ions coordinated in complexes are used in order to develop the understanding of paramagnetic NMR spectroscopy.



Ln(DOTA)$^-$



Ln(DO3A)

Ln = Eu^{3+}, Yb^{3+}, Tb^{3+}, Y^{3+}

[1] S. Faulkner, O. Blackburn, John Wiley & Sons, Inc. p., **2014**, 179-97.

Poster 37

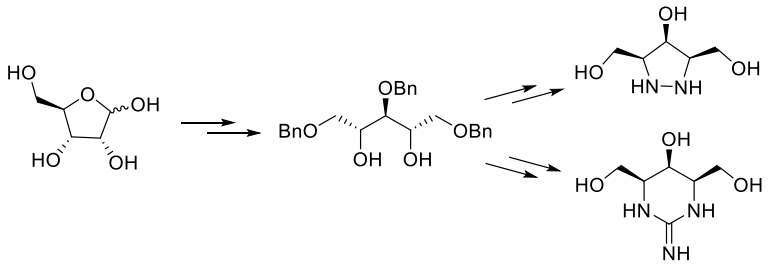
Pharmacological Chaperones against Krabbe Disease

Rikke F. Hansson, Helle H. Trinderup, and Henrik H. Jensen.

Department of Chemistry, Aarhus University, Langelandsgade 141, 1

8000 Aarhus, Denmark. au521796@post.au.com

This is an ongoing project with the aim of synthesizing 2 new compounds based on a joint synthetic route from D-Ribose. These compounds will hereafter be tested as pharmacological chaperones for the enzyme Galactocerebrosidase. This enzyme is in some cases of Krabbe disease misfolding, causing degradation of myelin sheaths around the axons resulting in death within the first two years after birth.



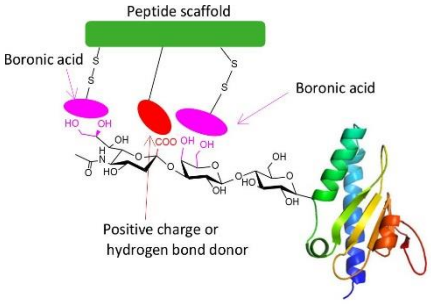
Poster 38

DEVELOPMENT OF RECEPTORS FOR AQUEOUS CARBOHYDRATE RECOGNITION

V. Baj[1,2], T. E. Nielsen[2], C. Behrens[2], and S. R. Beeren[1]

[1]Chemistry department, Technical University of Denmark, Kemitorvet Building 207, 2800 Kgs. Lyngby, Denmark.
[2]Department of Proteins and Peptides 3, Novo Nordisk, Novo Nordisk Park 1, 2760 Målov, Denmark.
vanbaj@kemi.dtu.dk

Sialic acids are anionic monosaccharides widely distributed in human tissues where they constitute the terminal residue of the oligosaccharides on glycoproteins. Sialylation is important to a protein´s function, physical properties and stability, and the ability to monitor the degree of sialylation is important in the development of protein-based drugs. In this project, we seek to develop synthetic receptors for sialic acid using dynamic combinatorial chemistry.



Here we present our investigation of sialic acid recognition by receptors that combine boronic acid and peptide recognition motifs. We have established optimized reaction conditions to generate disulfide-based dynamic combinatorial libraries and from templated dynamic combinatorial libraries we have identified receptors for sialic acid. We are currently exploring the importance of different amino-acid residues on binding affinity and conducting binding studies on the isolated receptors to quantify the strength of the interactions and examine the mode of binding.

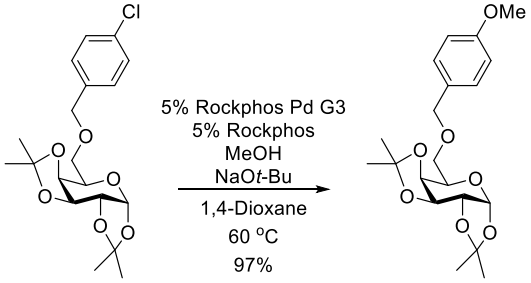
Poster 39

A NEW ROBUST ALCOHOL PROTECTING GROUP

Agnete H. Viuff, Mads Heuckendorff, and Henrik H. Jensen*.

Department of Chemistry, Aarhus University, Langelandsgade 140, 8210 Aarhus C, Denmark. hhj@chem.au.dk

The chemical synthesis of hydroxylated compounds such as carbohydrates requires the use of protecting groups that are robust against a wide range of conditions. Here we report the formation of the *p*-chloro-benzyl protecting group which can be converted into the much more labile *p*-methoxybenzyl group in one step using palladium catalysis.[1]



[1] Cheung, C. W.; Buchwald, S. L. *Org. Lett.* **2013**, *15*, 3998.

Poster 40

Palladium Catalyzed Carbonylative Double Trifluoromethylation

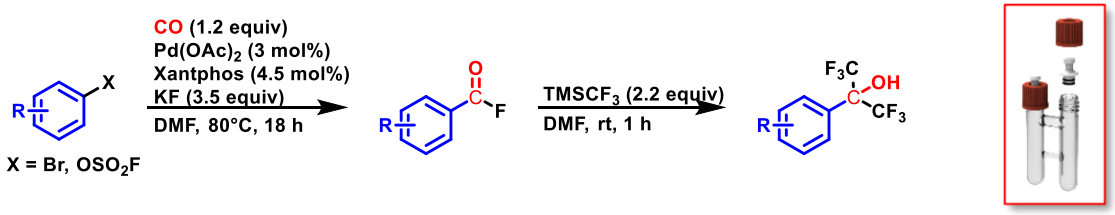
Katrine Domino and Troels Skrydstrup.

Aarhus University, Carbon Dioxide Activation Center (CADIAC), Department of Chemistry and the Interdisciplinary Nanoscience Center (iNANO), Gustav Wieds Vej 14, 8000 Aarhus C, Denmark.

domino@inano.au.dk

Introduction of fluorine atoms into organic molecules is an important strategy utilized in development of pharmaceuticals, agrochemicals and materials.

The aim of this project is to develop a new method for formation of HFIP substituted (hetero)arenes by a palladium-catalyzed carbonylative coupling which also allows for isotopic labelling by employing stoichiometric amounts of carbon monoxide.



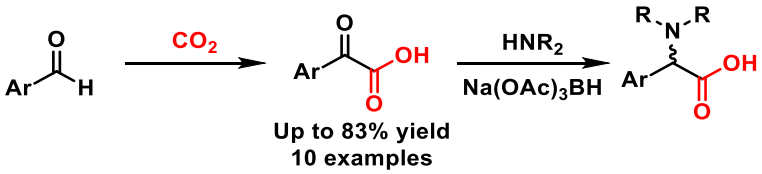
Poster 41

Carboxylation of aldehydes: Retrosynthesis of α-Amino Acids

Martin Juhl, Jiwoong Lee.

Department of Chemistry, University of Copenhagen, Universitetsparken 5, DK-2100 Copenhagen, Denmark.
Jiwoong.lee@chem.ku.dk

A novel carboxylation procedure has been developed enabling the formation of aryl keto-acids from the corresponding aldehydes using carbon dioxide as C1-building block. The procedure relies on Umpolung reactivity of aldehydes and in-situ retro-benzoin reaction affording keto-acid up to 83 % yield with good functional group tolerance. By a direct reductive amination an array of α-amino acids can be generated, proposing a new prebiotic synthesis of α-amino acids with carbon dioxide.



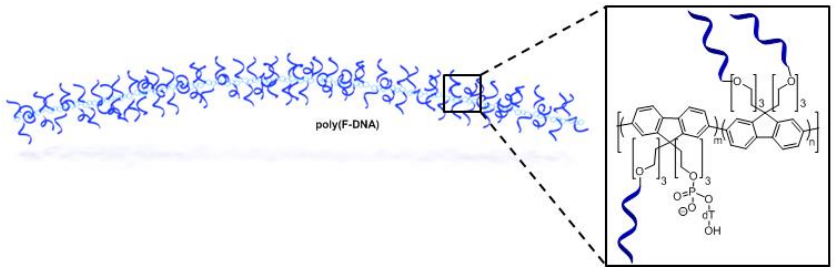
Poster 42

Manipulation of DNA-brushed conjugated polymers at the nanoscale

Mette R. Bakke, Mikael Madsen, and Kurt V. Gothelf.

iNANO, Department of Chemistry, Aarhus University, Gustav Wieds Vej 14, 8000 Aarhus C, Denmark.
m.bakke@inano.au.dk

The development of DNA-brushed conjugated polymers has allowed for single-molecule studies as well as high conformational control. By employing the DNA origami technique it is possible to control the relative positioning of two DNA-brushed polymers.[1] This will allow for analysis of energy transfer between conjugated polymers at the single-molecule level.



[1] M. Madsen, R. S. Christensen, A. Krissanaprasit, M. R. Bakke, C. F. Riber, K. S. Nielsen, A. N. Zelikin, and K. V. Gothelf, *Chem. Eur. J.,* **2017**, *13*, 10511-10515.

Poster 43

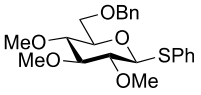
The Influence of Benzyl Groups on Anomeric Selectivity

Tatjana L. P. Sandgaard, and Henrik H. Jensen

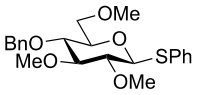
Department of Chemistry, Aarhus University, Langelandsgade 140, 8000 Aarhus C, Denmark

HHJ@chem.au.dk

The purpose is to synthesis two monobenzylated thioglycoside donors (**1**, **2**) with the desire of the donors being soluble in cold CH_2Cl_2 so it is possible to investigate their influence on the anomeric selectivity in a NIS/TfOH(cat) promoted glycosylation reaction.[1]



1



2

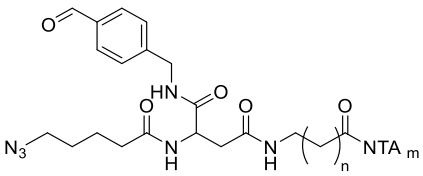
[1] M. Heuckendorff, L. T. Poulsen, H.H. Jensen, *J. Org. Chem.* 2016, *81*, 4988-5006

Poster 44

Site-selective bioconjugation of metal-binding proteins using small molecule probes

Nanna L. Nielsen, Michael R. Mortensen, Mikkel B. Skovgaard, Kurt V. Gothelf. Department of chemistry, iNANO center, Aarhus University, Gustav Wieds Vej 14, 8000 Aarhus, Denmark. Nanna.louise@live.dk

By using small molecule probes as seen below, we aim at labeling metal binding proteins including IgG1 antibodies in a site-selective manner. The probes contain nitrilotriacetic acid (NTA) groups as affinity groups, an aldehyde as reactive group for attachment of the probe to the protein, and an azide for attachment of the desired label using click chemistry. Several probes have been synthesized to determine how small structural variations can affect the yield and selectivity of the bioconjugation reaction.



Route to the Mathematical canteen from the department of Chemistry

Both the **dinner Friday** and **lunch Saturday** will be held at the mathematical canteen

TOKS XVI

Aarhus University 2017

Questions

Aske Donslund	28 56 28 13
Line Debois	31 22 84 10
Simon Laursen	27 28 39 15

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Emergency room	70 11 31 31
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Police	87 31 14 48